

Claims.

1. An implantable active agent delivery device for providing an active agent to a subject, the delivery device comprising a biomaterial comprising a volume of active agent having a front surface and a back surface, wherein the front surface of the biomaterial is adapted to be held substantially adjacent to vascular tissue within the subject; and wherein the biomaterial is capable of administering a biologically active agent or of providing a metabolic or immunologic function to the subject.
2. The device of claim 1 wherein the delivery device further comprises a tether for anchoring at an implantation site or retrieval after implantation.
3. The device of claim 2, wherein the tether is adapted to hold the biomaterial substantially adjacent to vascular tissue.
4. The device of claim 3, wherein the tether material is bioabsorbable.
5. The device of claim 3, wherein the tether is capable of serving as a means to replenish active agent within the device.
6. The device of claim 3 wherein the device further comprises a radio-opaque material.
7. The device of claim 3 wherein the device is adapted for delivery of active agent to the peritoneum.
8. The device of claim 3 wherein the device is adapted for delivery of active agent to the omentum.
9. The device of claim 7 or 8 wherein the delivery device is adapted for delivery through a cannula.
10. The device of claim 7 or 8 wherein the delivery device is a substantially flat sheet.

11. The device of claim 3, wherein the active agent is stable in the presence of elevated temperature or organic solvents.
12. The device of claim 1, 7 or 8 wherein the active agent is selected from the group consisting of antibodies, enzymes, trophic factors, growth factors, hormones and biological response modifiers.
13. The device of claim 1, 7 or 8 wherein the active agent is an analgesic or pain-reducing substance.
14. The device of claim 12, wherein the active agent is a peptide or protein.
15. The device of claim 14 wherein the active agent is a cytokine or lymphokine.
16. The device of claim 3, wherein the active agent is an immunogen.
17. The device of claim 3, wherein the active agent is prophylactic for use as a vaccine.
18. The device of claim 3, wherein the active agent comprises an antigen and an adjuvant.
19. The device of claim 3, wherein the biomaterial further comprises one or more delivery enhancing agents selected from the group consisting of polyethylene oxide (PEO), heparin, albumin, tissue growth factors, angiogenic growth factors, surfactants, anti-oxidants, anti-inflammatory agents, and anti-rejection medications.
20. The device of claim 3, wherein the angiogenic growth factor is selected from the group consisting of basic fibroblast growth factor, acidic fibroblast growth factor, vascular endothelial growth factor, platelet derived endothelial cell growth factor bb, angiopoietin-1, transforming growth factor beta, transforming growth factor alpha, hepatocyte growth factor, tumor necrosis factor-alpha, angiogenin, interleukin-8, hypoxia inducible

factor-i, angiotensin-converting enzyme inhibitor quinaprilat, angiotropin, thrombospondin, lactic acid, insulin, and growth hormone.

21. The device of claim 3, wherein the anti-inflammatory agent is selected from the group consisting of cortisone and ACTH, dexamethasone, cortisol, interleukin-1 and its receptor antagonists, and antibodies to TGF-beta, to interleukin-1 (IL-1), and to interferon-gamma.
22. The device of claim 3 wherein the device is adapted for delivery of active agent at a dose rate from about 0.001 to about 200 micrograms/hr.
23. The device of claim 3 wherein the device is adapted for delivery of active agent at a volume rate of from about 0.01 microliters/day to about 2 ml/day.
24. The device of claim 3, where the back surface of the biomaterial further comprises a substantially resilient substrate material capable of substantially maintaining the shape of the biomaterial.
25. The method of claim 3, wherein the biomaterial comprises a patch suitable for adhering to tissues.
26. The method of claim 25, wherein the patch further comprises (a) an impermeable backing layer; (b) an active agent layer element; and (c) an adhesive layer on the top surface for adhering to the tissues.
27. The device of claim 25 wherein the delivery device further comprises an active agent layer element having a hollow space and a top surface having a microporous or semi-permeable membrane.
28. The device of claim 25, further comprising a reservoir, wherein the reservoir contains active agent and is adapted to delivering the active agent to the front surface for delivery to the tissue.

29. The device of claim 25 wherein the device further comprises a penetration enhancer.
30. The device of claim 29, wherein the penetration enhancer is selected from the group consisting of cell-envelope disordering compounds, solvents and mixtures thereof.
31. The device of claim 3 wherein the delivery device further comprises an external selectively permeable jacket surrounding the core, the jacket comprising a biocompatible membrane having a molecular weight cutoff permitting passage of active agent molecules to and from the core through the jacket to provide the biological product or function.
32. The device of claim 31, wherein the molecular weight cutoff of the membrane is between about 50 - 2000 kD.
33. The device of claim 31 wherein the molecular weight cutoff of the membrane is above about 100 kD.
34. The device of claim 31 wherein the core comprises a biocompatible matrix formed from a hydrogel.
35. The device of claim 34, where the hydrogel is impregnated with pharmaceuticals.
36. The device of claim 31 wherein the jacket is selected from the group consisting of polyacrylonitrile-polyvinylchloride, polyacrylonitrile, polymethylmethacrylate, polyvinylidene fluoride, polyolefins, polysulfones and celluloses.
37. The device of claim 36 wherein the jacket further comprises a hydrophilic or hydrophobic additive.
38. The device of claim 3, where the biomaterial is a tissue matrix structure.

39. The device of claim 38, where the tissue matrix structure includes mammalian cells.
40. The device of claim 39 wherein the cells are allogeneic or syngeneic upon implantation.
41. The device of claim 39 wherein the cells are selected from the group consisting of insulin-producing cells, adrenal chromaffin cells, antibody-secreting cells, fibroblasts, astrocytes, Beta cell lines, and Chinese hamster ovary cells.
42. The device of claim 39 wherein the cells are insulin-producing cells.
43. The device of claim 39 wherein the cells secrete antibodies.
44. The device of claim 39 wherein all of the cells are disposed at a distance no greater than about 800 μm from the front face of the device.
45. The device of claim 39 wherein the delivery device further comprises a core comprising a volume in excess of 1 μl and at least about 10^4 living cells dispersed in a biocompatible hydrogel matrix, the cells being capable of secreting a active agent or of providing a metabolic or immunologic function.
46. The device of claim 39, further comprising a reservoir, wherein the reservoir contains nutrient-rich material and is adapted to delivering the nutrient-rich material to the cells.
47. The device of claim 39 wherein the cells are aggregated into a diffusional aggregate form adapted for increased packing per unit volume.
48. A method of implanting material into a subject, comprising the steps of (a) inserting a tethered active agent delivery device implant into the body of a subject; (b) releasing the delivery device the into the body near vascular tissue; (c) pulling the tether until the delivery device becomes substantially

adjacent to the vascular tissue; and (d) generally fixing the proximal end of the tether to substantially hold the delivery device substantially in contact with the vascular tissue; wherein the delivery device comprises a biomaterial comprising a volume of active agent and wherein the biomaterial is capable of administering a biologically active agent or of providing a metabolic or immunologic function to the subject.

49. The method of claim 48 wherein the administering is the delivery of a therapeutically effective amount.
50. The method of claim 49 wherein the therapeutically effective daily dose is from about 0.1 to about 100 mg/kg of body weight per day of active agent.
51. The method of claim 49 wherein the delivery of active agent is substantially continuous.
52. The method of claim 48 wherein the step of maintaining the contacting cells and composition under conditions and for a time sufficient to cause the cells to grow;
53. The method of claim 48 wherein the step of bringing into contact with tissues comprises administering the composition to a patient in need of such treatment a therapeutically effective amount of the active agent.
54. The method of claim 48 wherein the active agent is administered by implantation of the composition and wherein the substrate is shaped to match a desired tissue shape.
55. The method of claim 48 wherein the biomaterial is biodegradable.
56. The method of claim 48 wherein the biomaterial comprises an amount of the active agent sufficient for treatment of a subject for a period of at least about 3 days to about 10 days.

57. The method of claim 48 wherein the biomaterial comprises an amount of the active agent sufficient for treatment of a subject for a period of more than 20 days.
58. The method of claim 48 wherein the biomaterial comprises an amount of the active agent sufficient for treatment of a subject for a period of more than 30 days.
59. The method of claim 48 wherein the device is adapted for delivery of the active agent at a volume rate of from about 0.01 microliters per day to 3 milliliters per day.
60. The method of claim 48 wherein the device delivers the active agent at a rate of from about 0.01 micrograms of the active agent per hour to 300 micrograms of the active agent per hour.